REMARKS

Claims 1-3 and new Claims 4-13 remain active in the case. Reconsideration is respectfully requested.

Specification Amendment

The text has been amended on page 7 to correct a minor spelling error. Entry of the amendments and new claims is respectfully requested.

Claim Amendment

Claim 1-3 have been amended in order to improve upon the language of the claims. Further new Claims 4-9 have been added wherein Claims 4, 5 and 8 find support in original Claims 1-3 and are limited to peptide sequence I. Claims 6 and 7 find support in the specification on page 6 and new Claim 9 finds support on page 7 of the text. Claim 10 finds support in the test described with test mice on pages 10-12 of the text describing the attempted inducement of EAE in the mice having been administered peptide embodiments of the present invention . New Claims 11-13 are the same as Claims 1-3 except that the claims are limited to the peptide sequences of SEQ ID 1 and SEQ ID 4. Entry of the amendments and new claims is respectfully requested.

Claim Objections

The objection to Claim 2, line 14 is obviated by the amendment to the claim. As to the matter of the scope of the peptide sequences of Claims 1-3, applicants note that they have

presented new Claims 4, 5 and 8 which are limited to the elected peptide sequence I. Moreover, as addressed below, applicants maintain that there is a unity of invention among the four peptides.

Information Disclosure Statement

Applicants point out that copies of the two references cited in Form 1449 that have not been considered by the Examiner were, in fact, submitted to the Patent Office. However, in order to expedite consideration of these documents, applicants hereby enclose a copy of each reference.

Invention

The present invention finds its context in the area of treating a subject suffering from multiple sclerosis by the administration of a synthetic peptide which induces T cell anergy. The synthetic peptide corresponds to the major immunodominant T cell determinants of native protein antigens which area able to induce T cell unresponsiveness to themselves. This approach has not led to clinically useful results since altered peptides which are able to specifically act on the autoreactive T cell subset may cause the disease under certain conditions. Accordingly, the finding of the present invention is several peptides which induce a state of unresponsiveness of autoreactive T lymphocytes without inducing an autoreactive response. The peptide sequences of the present invention are selected from the group consisting of:

R-Asn-Gly-Val-Gly- His- Gly-Phe-Gly-Asn-Gly-Val-Gly-Pro-Gly-Thr-Gly-Pro-Gly-Ser-Gly-R′ (I) (SEQ ID NO: 1)

R-Gly-Pro-Gly- Val- Gly-Phe-Gly-Lys-Gly-Ile-Gly-Thr-Gly-Arg-Gly-Pro-Gly-Pro-Gly-Gln-R′ (II) (SEQ ID NO: 2)

R-Gln-Gly-Pro-Gly-Pro-Gly-Arg-Gly-Thr-Gly-Ile-Gly-Lys-Gly-Phe-Gly-Val-Gly-Pro-Gly-R′ (III) (SEQ ID NO: 3)

R-Gly-Ser-Gly- Pro- Gly-Thr-Gly-Pro-Gly-Val-Gly- Asn-Gly-Gly-Phe-Gly-His-Gly-Val-Gly-Asn-R′ (IV) (SEQ ID NO: 4)

where R is H- or $COCH_3$, R′ is COOH or $CONH_2$ and each amino acid has the L or D configuration.

Claim Rejection, 35 USC 112

Claim 3 stands rejected based on 35 USC 112 for failing to satisfy the enablement requirement. In this regard, the Examiner has noted that the text of the specification contains one example in which groups of test mice were administered peptides of sequences I and II, but then states that one of skill in the art would have to conduct undue or burdensome experimentation to implement the findings of the mice having induced EAE to a therapeutic treatment of human beings suffering from multiple sclerosis. However, applicants submit that it is clear from the discussion of relevant prior art in the text of the application that no such undue burden exists. That is, it is evident from the discussion on page 2 of the text that it is known that T lymphocytes are able to distinguish between substances belonging to the body (self) and foreign substances. Further, it is known that the T cell receptor can recognize modified ligands and respond in a variety of ways by different mechanisms which include T cell anergy. Anergy can be induced by synthetic peptides that correspond tho the major immunodominant T cell determinants of

native protein antigens which are able to induce T cell unresponsiveness to themselves. A known example is the substitution of proline (96→Pro) with alanine in the encephalitogenic peptide 87-99 Val-His-Phe-Phe-Lys-Ile-Val-Thr-Pro-Arg-Thr-Pro from human Myelin Basic Protein (hMBP). This change caused T cell hyporesponsiveness with a reduced ability to induce a proliferation response in a T cell clone specific for hMBP. It is then stated that this approach did not lead to clinically useful results. Thus it is clear that those of skill in the art were able to appreciate the state of clinical effectiveness of the peptide which means that these same individuals would not have been forced to undergo undue or burdensome testing involving the peptide in determining the effectiveness of the synthetic peptide for the treatment of human multiple sclerosis. This means also that one of skill in the art, having the disclosure of the present specification in hand which indicates the efficacy of two peptide embodiments of the invention in the prevention of the onset of EAE in test mice, would have no difficulty whatever in implementing clinical treatment of human beings suffering from multiple sclerosis using these peptides. Moreover, the present specification clearly provides disclosure as to forms in which the peptide embodiments can be administered to the human being and administered amounts that would be useful in effectively treating a subject.

Note also the disclosure in Karin et al, J. Exp. Med. 180(6), 2227-2237, where the authors state on page 2235, 2nd column that based on the test results of the incidence of the onset of EAE in test rats, clinical trials were conducted involving the administration of the MBP. Clearly, the skilled artisan, having information such as provided in the present specification, would have the wherewithal of implementing clinical treatment of human beings suffering from MS using the peptide embodiments of the present invention.

Further, as to the Examiner's comments concerning the necessity of submitting clinical trial results on human beings in order to demonstrate enablement, such is unfounded because clinical trials imply and require the disclosure of the drug(s) being tested which means that the identity of the drug(s) is (are) compromised. For this reason, pharmaceutical companies are compelled to base their search for the most efficacious drug on laboratory tests which are known to be as predictive as possible of the response that would be observed in treating human beings. In the case of the present invention, the *in vivo* assay of a drug on a susceptible strain of mice that is known to develop experimental autoimmune encephalomyelitis (Assay 1) is a Murine model of MS which is known to be predictive of the activity of a drug in man. (See page 7, lines 18-22 of the specification.) Thus, the tests reported in the present application represent the most proper and accurate experiments that could be conducted by applicant without compromising the novelty of the drug of the invention. Accordingly, the rejection based on a lack of enablement is believed overcome and withdrawal of the rejection is respectfully requested.

Restriction Requirement

Applicants maintain their position that there exists a unity of invention in the four peptides of the invention. As stated in Rule 1.475, the unity of invention requirement is fulfilled where there is a technical relationship among the inventions involving one or more of the same or corresponding special technical features. In the present case the claims directed to a peptide, a pharmaceutical composition containing the peptide and method of treating a subject suffering from multiple sclerosis with the peptide all have the same technical feature which is the four peptide types. Further, it is noted that the Examiner has stated that the amino acid sequences of

SEQ ID Nos. 1-4 are composed of different amino acids and are structurally and functionally unrelated to one another. (See the sentence bridging pages 2 and 3 of the Office Action.) This statement is erroneous because it should be observed that SEQ ID No. 3 and 4 are the reverse forms of the sequences of SEQ ID Nos. 1 and 2 respectively. Clearly, SEQ ID Nos. 1 and 4 are related since they contain the same amino acids, only in reverse order. The same thing is true for SEQ ID Nos. 2 and 3. Accordingly, there is a clear indication of unity in the invention and withdrawal of the requirement and consideration of all four peptides is requested, especially in light of the fact that no prior art rejection has been raised.

It is now believed that the application is in proper condition for allowance. Early notice to this effect is earnestly solicited.

Respectfully submitted,

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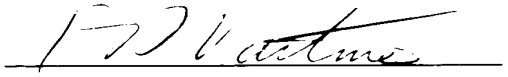

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